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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,796	03/13/2000	DOMINIQUE BRASSART	P99.2625	1391
29157	7590	11/04/2003	EXAMINER	
BELL, BOYD & LLOYD LLC			AFREMOVA, VERA	
P.O. BOX 1135				
CHICAGO, IL 60690-1135			ART UNIT	PAPER NUMBER

1651

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/445,796	Applicant(s) BRASSART ET AL.	
	Examiner Vera Afremova	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 11 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 11-14, 16-19 and 21-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 11-14, 16-19 and 21-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of claims

Claims 11-14, 16-19 and 21-26 as amended on 4/09/2003 [Paper No. 24] are pending and under examination in the instant office action.

Claims 1-10 were canceled by applicants in the Paper No. 10 filed 6/04/2001.

Claims 15 and 20 were canceled by applicants in the Paper No. 20 filed 9/03/2002.

Deposit

The deposit requirement for *Lactobacillus johnsonii* CNCM I-1225 has been met in the Paper No. 10 filed 6/04/2001.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-14 and 16-18 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,494,664.

Claims are directed to methods for treatment or prophylaxis of calcium deficiencies in a mammal at risk of calcium deficiency wherein the method comprises steps of enterally administering to the mammal at risk of calcium deficiency a nutritional composition comprising one or more live *Lactobacillus* bacteria. Some claims are further drawn to the use of *Lactobacillus sp.* CNCM I-1225 which is capable of adhering to intestinal cells in the method of administration of the nutritional composition. Some claims are further drawn to the use of milk products and/or milk hydrolysates in the nutritional composition in the method of administration.

Some claims are further drawn to the use of bacteria in amounts 10^7 to 10^{11} CFU/ml in the method of administration of the nutritional composition.

US 5,494,664 teaches a method for improving mammal health wherein the method comprises steps of enterally administering to a mammal a nutritional composition which contains live lactobacteria belonging to the genus of *Lactobacillus* including strain *Lactobacillus acidophilus (johnsonii)* CNCM I-1225 in amounts 10^7 to 10^8 CFU/ml in nutritional composition comprising yogurt and/or other milk-based ingredients. For example: see col. 1, line 43-60; col. 2, line 14; col. 4, lines 58-67).

The cited patent is considered to anticipate the claimed invention because the methods of the cited patent and of the present application are one active step protocols of enterally administering to identical patients an identical composition comprising identical amounts of identical bacteria belonging to the genus of *Lactobacillus* or strain CNCM I-1225 *Lactobacillus johnsonii* (previously identified as *acidophilus*) which is capable of adhering to intestinal cells. All mammalian patients including healthy patients of the cited patent are in need of calcium absorption for maintaining bone tissues and/or for maintaining general healthy state and, thus, the mammalian patients of the cited patent are considered to be identical to the patient at risk of calcium deficiency as in the claimed method. Consequently, the results/effects of practicing identical protocols of administering are reasonably expected to be identical at least as related to prophylaxis of calcium deficiency. The identical benefits are inherent to the identical administration. Therefore, the methods are identical as taught by the cited patent and as presently claimed.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1651

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11, 12, 16-19, 21, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sellars R.L. [ref. U-19 which is "Acidophilus Products". In: "Therapeutic properties of fermented milk". 1991, 81-116] and Yaeshima [ref. IDS-3-AR which is Bulletin of the International Dairy Federation. 1996, No. 313, 36-42].

Claims are directed to methods for prophylaxis or treatment of calcium deficiencies and for improving absorption of calcium by administering a nutritional composition comprising one or more live bacteria belonging to the genus of *Lactobacillus* to mammal patients at risk of calcium deficiency or in need of increased calcium absorption. Some claims are further drawn to the use of bacteria capable of adhering to intestinal cells. Some claims are further drawn to the use of milk products and/or milk hydrolysates in the nutritional composition in the method of administration.

The reference by Sellars teaches that consumption of "acidophilus" products with sufficient numbers of active viable cells promote mineral absorption (page 100, par. 3, lines 3-6) and that the fermented dairy products containing live "lactobacilli" bacteria increase mineral absorption (page 102, par. 2, lines 1-4). Thus, the cited reference clearly teaches and suggests methods for treatment of mineral deficiencies and for improving mineral absorption by administration of nutritional compositions comprising live "lactobacilli" bacteria of the "acidophilus" products. The "lactobacilli" bacteria of the "acidophilus" products in the reference by Sellars are bacteria belonging to the genus of *Lactobacillus* including *Lactobacillus acidophilus* and others including *Bifidobacterium*, for example: see table see tables I-III at pages 84-86. The reference by Sellars teaches that colonization of gastrointestinal tract (GI) by the "lactobacilli" bacteria of the "acidophilus" products bacteria promote mineral absorption (page

100, par. 3, lines 5-6). The cited reference by Sellars teaches benefits related to absorption of minerals in general but it is lacking particular disclosure about mineral calcium.

However, the reference by Yaeshima [IDS-3-AR] teaches the method for treatment and/or improving absorption of mineral that is calcium by administering to mammals the live cells of *Bifidobacterium* which is representative of “lactobacilli” contained in “acidophilus” products. The reference clearly demonstrates that enteral administration or consumption of the live “lactobacilli” contained in the “acidophilus” bacteria improves calcium absorption and increases bone strength. For example: see page 41, col. 1-2; Fig. 13; page 41, col. 2, lines 3-5. The reference by Yaeshima also teaches that the representatives of the whole group of the lactic bacteria including both “bifidobacteria” and “lactobacilli” are typical examples of beneficial bacteria residing in the intestines that contribute to digestion and absorption (page 36, col. 1, par. 1-2).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use live lactic bacteria of the genus *Lactobacillus* for administration to mammals at risk of calcium deficiency or in need of increased calcium absorption with a reasonable expectation of success in treating calcium deficiency and/or improving calcium absorption because consumption of live lactic bacteria including both *Lactobacillus* and *Bifidobacterium* promotes and increases mineral absorption and because the representatives of the whole group of lactic bacteria have demonstrated to increase calcium absorption. One of skill in the art would have been motivated to administer live lactic bacteria to mammals having mineral deficiency including calcium deficiency or to mammals requiring increase mineral absorption including calcium absorption for the expected benefits in treating mineral deficiency including calcium deficiency and/or improving mineral absorption including calcium absorption. One of skill in the art is free to select beneficial bacteria from the whole group of lactic bacteria since the whole group of lactic bacteria is regarded as being beneficial

for mineral absorption including calcium absorption. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. Further, it is considered to be within the skills of an ordinary practitioner in the field to use the additional components including milk protein hydrolysates or prebiotic fibers in the nutritional compositions intended for treatment or prophylaxis of mineral deficiencies including calcium deficiencies or for improving absorption of calcium from diets depending on patient age, life style and/or general state of health. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Claims 11-14, 16-19 and 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sellars R.L. and Yaeshima as applied to claims 11, 12, 16-19, 21, 23 and 24 above, and further in view of US 5,494,664 and US 5,578,302.

Claims 11, 12, 16-21, 23 and 24 as explained above. Some claims are further drawn to the use of bacteria capable of adhering to intestinal cells or particular strain CNCM I-1225 belonging to *Lactobacillus johnsonii* (priorly identified as *acidophilus*). Some claims are further drawn to the use of bacteria in amounts 10^7 to 10^{11} CFU/ml in the method of administration of the nutritional composition.

Both cited references by Sellars and by Yaeshima teach that the benefits related to mineral absorption including calcium absorption are the result of administration of lactic bacteria. But they are lacking particular disclosure related to the use of a particular lactic bacterium which is strain CNCM I-1225 *Lactobacillus johnsonii*.

However, the cited US 5,494,664 and US 5,578,302 discloses the therapeutic use of the particular strain CNCM I-1225 *Lactobacillus johnsonii* (previously identified as *acidophilus*)

which is capable to colonize GI and to adhere to intestinal cells and which promotes health benefits in mammals. The therapeutic applications in the cited patents are based on GI colonization by lactic bacteria and, in particular, by bacterial cells of the strain CNCM I-1225 *Lactobacillus johnsonii*.

The cited reference by Sellars teaches that the colonization of gastrointestinal tract by the lactic bacteria promotes and increases mineral absorption. The cited reference by Yaeshima teaches that the residence or the establishment of lactic bacteria in the intestines of mammals promotes health benefits and increases calcium absorption and bone strength. But the cited references by Sellars and by Yaeshima are silent about the particular amounts which are required for GI colonization.

However, the cited US 5,494,664 teaches the particular amounts of live bacterial cells including the strain CNCM I-1225 such as 10^7 to 10^{11} CFU/ml which provide for GI colonization and for bacterial residence in intestines (col. 4, lines 66-67, col. 3, lines 1-3 and 22-25). The cited patent US 5,494,664 also teaches that traditional yogurt, which is one of the “acidophilus” product of the reference by Sellars, is believed to provide for the similar amounts of lactic bacteria (col. 3, lines 35-37) that are sufficient to establish residence or colonize GI.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use live bacteria of the strain CNCM I-1225, which is *Lactobacillus johnsonii* (priority identified as *acidophilus*), in the method of administering to mammals in needs of mineral absorption including calcium absorption with a reasonable expectation of success in treating mineral deficiencies including calcium deficiency in mammals and/or improving absorption of minerals including calcium in mammals because bacteria from the same group of lactic bacteria have been taught and/or suggested for the same purpose of improving mineral absorption including calcium absorption as adequately demonstrated by these cited references by Sellars and by Yaeshima. One having ordinary skill in the art would have

been motivated to use the strain CNCM I-1225 because this strain has been taught as capable to colonize GI and the colonization of GI promotes mineral absorption including calcium absorption. One having ordinary skill in the art would have been motivated to use about 10^7 to 10^{11} CFU/ml amounts of lactic bacteria in the compositions in the methods in treating mineral deficiencies including calcium deficiency in mammals and/or improving absorption of minerals including calcium from diets because the prior art teaches that these amounts of lactic bacteria are sufficient for GI colonization and because the GI colonization promotes mineral absorption including calcium absorption as adequately demonstrated by the cited prior art. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants' arguments filed 8/11/2003 have been fully considered but they are not persuasive.

Applicants argue that the anticipation rejection is improper (response page 2-4).

Although the cited US '664 is silent with respect to the particular effects as claimed, the inherent effect of the one step of administering lactobacillus would reasonably be assumed to be the same effects as claimed because the patient is the same, the step of enterally administering is the same and the same bacterial composition is administered in the same amount. Thus, the result should be the same that is prophylaxis or eliminating of risk of calcium deficiency.

Applicants appears to argue that the *Lactobacillus* of the cited patent is not capable of "arriving in a living state" in intestines. This is not found persuasive because the cited patent teaches the use of identical bacteria as claimed and, thus, it is inherently capable of the same

properties or function. Moreover, the cited patent US'664 teaches the GI colonization by the administered lactic bacteria and, thus, the bacteria are reasonably assumed to be living to achieve the GI colonization.

Applicants appears to argue that the specification example 1 discloses a surprisingly new properties or function related to improvement of mineral absorption as result of direct interaction between the claimed bacteria and the intestinal cells. However, a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

With regard to the claim rejection under 35 U.S.C. § 103 applicants argue (response pages 5-8) that the cited patents US 5,494,664 and US 5,578,302 do not suggest capability of lactobacteria to improve absorption of calcium from the diets and that the references by Sellars and by Yaeshima teach away from the applicants' invention by suggesting the beneficial role of other ingredients (lactic acid, lactose, vitamins) in the improvement of mineral absorption (response pages 5-7).

Applicants' argument with respect to the discovery about mineral absorption as result of direct interaction between the intestinal cells of the Caco-2 cell line model and the living cells by bacteria including the strain taught in US 5,494,664 and US 5,578,302 as disclosed on page 9 of the instant specification have been fully considered. Although the cited patents US 5,494,664 and US 5,578,302 are silent about mineral absorption, they teach the therapeutic use of the same bacteria as presently claimed wherein the therapeutic use is based on GI colonization by the lactic bacteria or on direct contact with the intestinal cells of patients. Thus, the inherent properties of lactic bacteria including the presently claimed strain which is taught in US 5,494,664 and US 5,578,302 would provide for the mineral absorption effects upon GI colonization after administration in the same amounts which are taught by the cited patent US 5,494,664 as therapeutically effective amount for the treatments based on GI colonization by

lactic bacteria. The reference by Sellars clearly teaches that the GI colonization by live lactic bacteria promotes the mineral absorption. Thus, the invention as a whole would have been obvious under 35 U.S.C. 103.

With regard to the reference by Sellars applicants appears to argue that it discloses the role of metabolites of fermenting lactic bacteria in mineral absorption. However, the cited reference also clearly teaches that the GI colonization by lactic bacteria derived from “acidophilus” products promotes and increases mineral absorption.

With regard to the reference by Yaeshima applicants appear to argue that *Bifidobacterium* and *Lactobacillus* are non-related bacteria. This is not true. The bacteria belonging to *Bifidobacterium* and *Lactobacillus* are both beneficial lactic bacteria of the “acidophilus” products and they promote mineral absorption as clearly demonstrated by Sellars (tables I-III). Moreover, the reference by Yaeshima regards both bifidobacteria and lactobacilli as typical examples of microflora residing in mammalian intestines that contributes to digestion and absorption. Applicants’ arguments that the Fig. 13 of the reference by Yaeshima fails to teach/suggest the use of bacteria for increasing calcium absorption is not found convincing. The Fig. 13 clearly demonstrates that the strength of bones increases when bacteria are added to the calcium containing diet. Thus, the use of lactic acid bacteria increases calcium absorption.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

No claims are allowed.

Art Unit: 1651

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

Art Unit 1651
October 30, 2003

VERA AFREMOVA
PATENT EXAMINER

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.